

## CLAIMS

What is Claimed Is:

5           1. A substantially pure DNA sequence encoding acetylcholinesterase (AChE) selected from the group consisting of:

(a) genomic clones having a nucleotide sequence derived from the genomic region of a human AChE gene;

10           (b) cDNA clones having a nucleotide sequence derived from the sequence of said genomic clones of (a);

(c) DNA sequences capable of hybridization to the clones of (a) and (b) under moderately stringent conditions and which encode biologically active AChE; and

15           (d) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences defined in (a), (b) and (c) and which encode biologically active AChE for use in biopharming.

20           2. A DNA sequence according to claim 1, wherein said sequence encodes human AChE or biologically active derivatives thereof.

25           3. A DNA sequence according to claim 2, which has all or part of the nucleotide sequence substantially as depicted in Fig. 1A, (SEQ ID NO:1) and which encodes an amino acid sequence substantially similar or identical to  
30 all or part of the sequence of amino acid residues depicted in Fig. 1B (SEQ ID NO:2).

4. A DNA sequence according to claim 2, which has all or part of the nucleotide (SEQ ID NO:3) sequences substantially as depicted in Fig. 1C, and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:4) also depicted in Fig. 1C.

5. A DNA sequence according to claim 2, which has all or part of the nucleotide sequence (SEQ ID NO:5) substantially as depicted in Fig. 1D, and which encodes an amino acid sequence (SEQ ID NO:6) substantially similar or identical to all or part of the sequence of amino acid residues also depicted in Fig. 1D.

6. A recombinant expression vector comprising a DNA sequence according to claim 1.

7. A recombinant expression vector for use in biopharming, according to claim 6 which has a DNA sequence encoding a human AChE or biologically active derivatives thereof selected from:

(a) a DNA sequence which has all or part of the nucleotide sequence (SEQ ID NO:1) substantially as depicted in Fig. 1A, and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:2) depicted in Fig. 1B;

(b) a DNA sequence which has all or part of the nucleotide sequences substantially as depicted in Fig. 1C, and which encodes an amino acid sequence substantially

similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:3) also depicted in Fig. 1C; and

5 (c) a DNA sequence which has all or part of the nucleotide sequence (SEQ ID NO:5) substantially as depicted in Fig. 1D, and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:6) also depicted in Fig. 1D;

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8. A recombinant expression vector according to claim 7, which has a promoter controlling the transcription of said sequence encoding AChE selected from the group of eukaryotic host cell compatible promoters consisting of CMV, CMV-like, AChE and AChE-like promoters.

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9. A eukaryotic host cell transformed with the expression vector according to claim 6, said host cell being capable of expressing AChE when cultured under conditions promoting AChE expression.

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10. A eukaryotic host cell transformed with the expression vector according to claim 7, said host cell being capable of expressing AChE when cultured under conditions promoting AChE expression.

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11. A transgenic animal carrying a recombinant DNA expression vector encoding a heterologous cholinesterase (ChE) enzyme selected from the group consisting of:

- 5 (a) normal human AChE;  
(b) normal human BChE;  
(c) naturally-occurring variants of the AChE and BChE of (a) and (b);  
(d) synthetic variants of the AChE and BChE of  
10 (a) and (b), said synthetic variants selected from recombinantly-produced point-mutated and deletion, of one or more residues, mutations; and  
(e) normal insect ChEs, said transgenic animal being capable of expressing substantial amounts of said ChE  
15 enzyme for studying control of production on biochemical properties of cholinesterases.

20 12. A transgenic animal according to claim 11 selected from *Xenopus* and mice.

25 13. A transgenic animal according to claim 12, which carrying a recombinant expression vector encoding a human AChE or biologically active derivatives thereof selected from:

- 30 (a) a DNA sequence which has all or part of the nucleotide sequence (SEQ ID NO:1) substantially as depicted in Fig. 1A, and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:20) depicted in Fig. 1B;

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5 (b) a DNA sequence which has all or part of the nucleotide sequences (SEQ ID NO:3) substantially as depicted in Fig. 1C, and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:4) also depicted in Fig. 1C; and

10 (c) a DNA sequence which has all or part of the nucleotide sequence (SEQ ID NO:5) substantially as depicted in Fig. 1D, and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:6) also depicted in Fig. 1D.

15 14. A transgenic animal according to claim 13, in which said recombinant expression vector contains a promoter controlling the transcription of said sequence encoding AChE selected from the group of eukaryotic host cell compatible promoters.

20 15. Acetylcholinesterase produced by a eukaryotic host cell according to claim 9.

25 16. Acetylcholinesterase produced by a eukaryotic host cell according to claim 10.

Sub A2 30 17. A transgenic animal assay system for studying secretion, control of production and biochemical properties of cholinesterases in mammalian milk, comprising a transgenic mammal according to claim 11.

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18. A transgenic mammal according to claim 11, being capable of expressing substantial amounts of ChE enzyme in its mammary glands.

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19. The transgenic animal according to claim 18, wherein said ChE enzyme is selected from the group consisting essentially of normal human AChE, naturally-occurring variants of AChE, and synthetic variants of the AChE.

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20. The transgenic animal according to claim 19, wherein said synthetic variants are selected from the group consisting essentially of recombinantly-produced point mutation and deletion of one or more residues and mutations.

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21. A method of treatment of acute traumatic injury by administering to a patient in need of such treatment a therapeutically effective amount of at least one of an antisense oligodeoxynucleotide selected from the group consisting essentially of Seq. ID. No. 1-6.

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22. The method according to claim 21, wherein said administration step further results in preventing AChER overproduction and excessive dendritic growth.

23. A transgenic female mammal according to claim 23 wherein said ChE enzyme is selected from the group consisting of:

- 5 (i) normal human AChE;  
(ii) naturally occurring variants of AChE of claim 23; and  
(iii) synthetic variants of the AChE of claim 23, said synthetic variants selected from recombinantly produced point mutated and deletion of one or more residues and  
10 mutations.

24. A method of producing recombinant human AChE comprising the steps of:

- 15 (i) providing a lactating transgenic animal according to claims 23 or 24;  
(ii) obtaining milk from the animal; and  
(iii) isolating from the milk obtained in step (ii) human AChE.  
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25. The transgenic animal according to claim 11 which has all or part of the nucleotide sequence (Seq. ID 28).